Cardiocerebral Resuscitation Is Associated With Improved Survival and Neurologic Outcome from Out-of-hospital Cardiac Arrest in Elders

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Abstract

Background: Recent studies have shown that a new emergency medical services (EMS) protocol for treating patients who suffer out-of-hospital cardiac arrest (OHCA), cardiocerebral resuscitation (CCR), significantly improves survival compared to standard advanced life support (ALS). However, due to their different physiology, it is unclear if all elders, or any subsets of elders who are OHCA victims, would benefit from the CCR protocol.

Objectives: The objectives of this analysis were to compare survival by age group for patients receiving CCR and ALS, to evaluate their neurologic outcome, and to determine what other factors affect survival in the subset of patients who do receive CCR.

Methods: An analysis was performed of 3,515 OHCAs occurring between January 2005 and September 2008 in the Save Hearts in Arizona Registry. A total of 1,024 of these patients received CCR. Pediatric patients and arrests due to drowning, respiratory, or traumatic causes were excluded. The registry included data from 62 EMS agencies, some of which instituted CCR. Outcome measures included survival to hospital discharge and cerebral performance category (CPC) scores. Logistic regression evaluated outcomes in patients who received CCR versus standard ALS across age groups, adjusted for known potential confounders, including bystander cardiopulmonary resuscitation (CPR), witnessed arrest, EMS dispatch-to-arrival time, ventricular fibrillation (Vfib), and agonal respirations on EMS arrival. Predictors of survival evaluated included age, sex, location, bystander CPR, witnessed arrest, Vfib/ventricular tachycardia (Vtach), response time, and agonal breathing, based on bivariate results. Backward stepwise selection was used to confirm predictors of survival. These predictors were then analyzed with logistic regression by age category per 10 years of age.

Results: Individuals who received CCR had better outcomes across age groups. The increase in survival for the subgroup with a witnessed Vfib was most prominent on those <40 years of age (3.7% for standard ALS patients vs. 19% for CCR patients, odds ratio [OR] = 5.94, 95% confidence interval [CI] = 1.82 to 19.26). This mortality benefit declined with age until the ≥80 years age group, which regained the benefit (1.8% vs. 4.6%, OR = 2.56, 95% CI = 1.10 to 5.97). Neurologic outcomes were also better in the patients who received CCR (OR = 6.64, 95% CI = 1.31 to 32.8). Within the subgroup that received CCR, the factors most predictive of improved survival included witnessed arrest, initial rhythm of Vfib/Vtach, agonal respirations upon arrival, EMS response time, and age. Neurologic outcome was not adversely affected by age.

Conclusions: Cardiocerebral resuscitation is associated with better survival from OHCA in most age groups. The majority of patients in all age groups who survived to hospital discharge and who could be reached for follow-up had good neurologic outcome. Among patients receiving CCR for OHCA, witnessed arrest, Vfib/Vtach, agonal respirations, and early response time are significant predictors of survival, and these do not change significantly based on age.

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Keywords: cardiocerebral resuscitation, CPR, geriatric, cardiac arrest

Out-of-hospital cardiac arrest (OHCA) is a devastating event with dismal mortality.[1–5] The incidence of treated OHCA in the United States is estimated to be 52 per 100,000 population, or almost 300,000 arrests per year, with survival to hospital discharge ranging widely from 3.0% to 16.2%.[6] With the aging of our population, an estimated 22% of our population will be over 65 years of age by 2030, and the current number of elder patients treated for cardiac arrest annually can be expected to increase proportionally.[7] Advances in the treatment of patients in cardiac arrest depend on a well functioning chain of survival, including bystander cardiopulmonary resuscitation (CPR), early defibrillation with public access, and emergency medical services (EMS) protocols for advanced cardiac life support (ACLS). Also needed is optimal postarrest care, including therapeutic hypothermia and early percutaneous coronary intervention.[8,9]

Based on decades of resuscitation research, experts at the University of Arizona Sarver Heart Center developed an EMS protocol termed cardiocerebral resuscitation (CCR).[10–22] This protocol emphasizes high quality, minimally interrupted chest compressions, delayed active ventilation, and early epinephrine administration. It was adopted by several EMS systems in Arizona and has shown overall improved survival to hospital discharge, especially in the subgroup with witnessed ventricular fibrillation (Vfib).[17,18,22]

To date, no analysis has been done on the effect of CCR on survival rates across age groups. Older patients have a lower incidence of Vfib arrests and more comorbidities, both negatively affecting their likelihood for survival.[23–26] As the underlying etiologies of OHCA in elders often differ from those in their younger counterparts, the question is raised: is resuscitation in elders futile, and do different resuscitative measures need to be taken? The primary objective of this analysis was to determine if survival and neurologic outcome benefits exist with patients across age groups who received CCR compared to standard ACLS. Secondarily, we looked specifically at those patients who received CCR and analyzed what factors affected survival.

METHODS

Study Design
This was a retrospective analysis of a cardiac arrest quality improvement database. In 2004, the Arizona Department of Health Services, Bureau of Emergency Medical Services and Trauma System developed the Save Hearts in Arizona Registry and Education (SHARE) database to address OHCA as a public health problem. This initiative is a statewide quality improvement program with data exemption from the Health Insurance Portability and Accountability Act. The Arizona Department of Health Services, Human Subjects Review Board, and the University of Arizona Institutional Review Board granted permission to publish deidentified SHARE program data and contact OHCA survivors for follow-up evaluation.

Study Setting and Population
Sixty-two Arizona EMS agencies covering approximately 80% of the state population participate in the SHARE program, as previously described.[27]

Study Protocol
Utstein-style information was gathered on patient demographics, event circumstances, response intervals, presenting rhythm, bystander CPR, treatment and procedures, and initial outcomes from EMS providers.[28] Final outcomes were then obtained via local hospitals and the Bureau of Public Health Statistics. An analysis of all eligible OHCAs between January 1, 2005, and September 30, 2008, in the SHARE Registry was performed. Analysis of the total database between January 1, 2005, and November 22, 2007, comparing CCR and standard ACLS EMS care was previously reported.[17] This analysis extends the time period to September 30, 2008, and assesses survival across age groups.

Cardiac arrest was defined by an absence of cardiac mechanical activity based on pulselessness and cessation of normal breathing. An initiation of resuscitation was required for inclusion into the database. Documented rhythms by EMS included asystole, pulseless electrical activity, Vfib, and ventricular tachycardia (Vtach). Patients with obvious signs of death, such as rigor mortis and lividity, and those with documented do not attempt resuscitation (DNAR) wishes were excluded, as resuscitative measures were not begun. Children under 18 years of age, arrests witnessed by the medics, and presumed noncardiac etiologies of the arrest were excluded from the primary analysis.

The new CCR protocol was presented to EMS directors throughout the state, and they were given the option of instituting CCR in their systems. Over the 3-year period under analysis, approximately 30 of the 62 EMS systems participating in the SHARE Registry elected to implement CCR. CCR training was provided using a train-the-trainer model. Trainers in participating EMS systems were given written materials, slides, and verbal and psychomotor instruction.

The CCR protocol was defined a priori as 1) initiation of 200 immediate, uninterrupted chest compressions at a rate of 100 compressions/min; 2) analyzing the rhythm and delivering a single defibrillator shock, if indicated; 3) 200 more chest compressions before the first pulse check or rhythm reanalysis; 4) epinephrine (1 mg intravenous or intraosseous) as soon as possible or with each 200 compression cycle; or 5) endotracheal intubation delayed until after three cycles of chest compressions.[17]

Outcome Measures
The primary outcome measures were survival to hospital discharge and cerebral performance category (CPC) scores among survivors.[28,29] Once survival to hospital discharge was confirmed, a letter was sent to the patient. If no response was returned, a second letter was sent. If there was no reply at that time, no further attempt was made, but hospital discharge CPC was obtained from the medical record when available. If an affirmative reply was returned from the letters, a

telephone survey was conducted. Extremely good neurologic outcome (conscious, alert, able to work, possibly mild neurologic or psychological deficit) received a CPC score of 1. A score of 2 was given to those patients who were conscious, had sufficient cerebral function for independent activities of daily living (ADL), and could work in a protected environment. A ''3'' was assigned to those with severe cerebral limitation and were conscious, but dependent on others for their ADLs, severe dementia, or paralysis. A ''4'' was assigned to those in a coma or a vegetative state. In our analysis, those patients who received a CPC score of 1 or 2 were considered to have a favorable neurologic outcome.

Data Analysis

The association between CCR and survival was evaluated with odds ratios (ORs) and 95% confidence intervals (CIs). We performed the same analysis in the subset of the cohort that experienced witnessed arrest and had Vfib or Vtach. In the analysis of CCR and survival in the total sample, and for the age 65 years and above and the below age 65 years subsamples, ORs and 95% CIs were estimated using logistic regression. An interaction term (age 65 years and above by CCR status) was included in the model for total sample analysis. In the analysis of CCR and survival by decade of age stratum, ORs and 95% CIs were calculated via 2×2 contingency tables (the cross-product) and the Cornfield method for deriving the 95% CI (Stata version 10, StataCorp, College Station, TX).

The proportion of survivors with intact neurologic function was compared between CCR and standard ACLS with the Fisher's exact test, and the adjusted OR was derived with logistic regression, with neurologic outcome as the dependent variable. We examined predictors of survival in the 1,024 patients who received CCR using logistic regression, with survival to discharge as the dependent variable. Potential predictors were entered into logistic models if they had bivariate associations with the dependent variable with p < 0.10 or if they were theorized to play an important role. Variables tested were age, sex, location of cardiac arrest, bystander present, witnessed arrest with Vfib/Vtach initial rhythm, agonal respirations, and EMS response time. Interaction terms were constructed between age and each main effect (witnessed arrest, Vfib/Vtach, agonal respirations, and EMS response time), by multiplying age and the main effect. Independent predictor variables were retained in the model if p < 0.05.

RESULTS

A total of 5,000 patients were logged into the registry between January 2005 and September 2008. Of these, 1,485 were children, had noncardiac causes of cardiac arrest, or met other exclusion criteria (Figure 1). The remaining 3,515 adult patients with OHCA were analyzed, 2,491 (71%) received standard ACLS, and 1,024 (29%) received CCR (Figure 1). Among the subset of patients who experienced witnessed Vfib or Vtach arrest, 547 (71%) received standard ACLS and 219
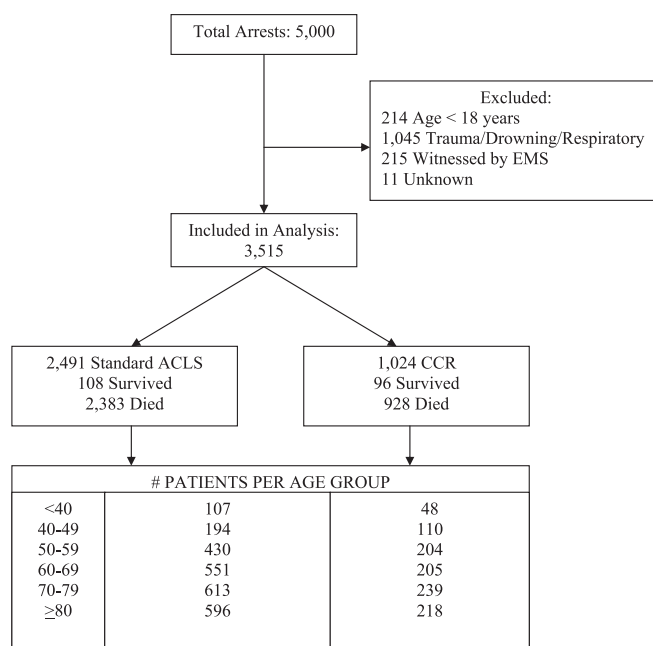

Figure 1. Distribution of patients. ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; EMS = emergency medical services.

(29%) received CCR. Demographic and arrest variables were not significantly different between the CCR and standard ACLS groups (Table 1).

In all patients, the out-of-hospital survival was 5.8%. Individuals who received CCR had higher survival

Table 1
Patient Demographics

	CCR	Standard ACLS
Number	1,024	2,491
Age (yr), mean (±SD)	66 (±15)	67 (±15)
Male	690 (67)	1619 (65)
Female	334 (33)	872 (35)
Location		
Home	722 (70)	1660 (66.6)
Clinic	12 (1.2)	67 (2.7)
Long-term care	145 (14)	332 (13)
Public	145 (14)	432 (17)
Witnessed arrest	450 (44)	1121 (45)
Bystander CPR	415 (41)	1000 (40)
Time to EMS arrival (min), mean ± SD	5.3 (±2.3)	5.8 (±3.7)
Vfib/Vtach arrest	315 (31)	785 (32)
Initial rhythm		
Asystole	498 (48)	1196 (48)
PEA	209 (20)	508 (20)
Sinus bradycardia	0 (0)	1 (0.04)
Sinus tachycardia	1 (0.10)	0 (0)
Vfib	315 (31)	778 (31)
Vtach	0 (0)	7 (0.28)
Other	1 (0.10)	0 (0)

Values are n (%) unless otherwise noted.
ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; CPR = cardiopulmonary resuscitation; EMS = emergency medical services; PEA = pulseless electrical activity; Vfib = ventricular fibrillation; Vtach = ventricular tachycardia.

Table 2
Survival Benefit Associated With CCR

	Unadjusted OR	95% CI	Adjusted* OR	95% CI
Total sample	3.0	2.05–4.49	3.1	1.96–4.76
Age less than 65 yr	3.0	2.05–4.49	3.1	1.99–4.88
Age 65 yr and above	1.5	0.98–2.36	1.9	1.18–3.16
Age-by-CCR interaction (p-value)	0.02	NA	0.15	NA

*Adjusted for witnessed arrest, Vfib/Vtach, agonal respirations, EMS response time, and age over 65 years (for total sample only).
CCR = cardiocerebral resuscitation; EMS = emergency medical services; OR = odds ratio; Vfib = ventricular fibrillation; Vtach = ventricular tachycardia.

overall both above and below age 65 years (Table 2). When stratified by decade of age, except for the 70–79 years age group, the survival benefit remained for all arrests, and the witnessed Vfib/Vtach arrests, compared to those patients who received standard ACLS (Tables 3 and 4). The OR for the increase for survival was highest for patients under age 40 years (Figure 2).

In the subset of 1,024 patients who received CCR, independent predictors of survival included witnessed arrest (OR = 3.3, 95% CI = 1.8 to 6.1), Vfib/Vtach (OR = 7.0, 95% CI = 3.9 to 12.5), agonal respirations (OR = 4.6, 95% CI = 2.6 to 8.2), EMS response time (for each addi-

tional minute, OR = 0.87, 95% CI = 0.76 to 0.99), and age (for each additional 10 years, OR = 0.79, 95% CI = 0.67 to 0.93; Table 5). Age appears to have a linear relationship with the log-odds of survival without effect modification (interaction) with other predictors.

Neurologic outcomes data were collected on 147 of the 204 survivors (72%). Patients who received CCR had significantly better neurologic outcome than those receiving standard ACLS, with 96.6% in the CCR group and 85% in the standard ACLS group (Table 6). Adjusted for witnessed arrest and presence of Vfib/Vtach initial rhythm, the CCR group had more than six times greater likelihood of a favorable neurological outcome (OR = 6.54, 95% CI = 1.31 to 32.8). Because of the small number of survivors in each of the age groups, we did not have enough power to reach statistical significance when assessing neurologic outcome across age groups.

Table 3
Survival After Standard ACLS Versus CCR, Stratified by Age Groups

| Age (yr) | Percent Survival | | OR | 95% CI |
	ACLS	CCR		
<40	3.74	18.75	5.94	1.82–19.26
40–49	5.67	16.36	3.25	1.50–7.07
50–59	5.35	11.27	2.25	1.24–4.09
60–69	5.99	10.24	1.79	1.02–3.16
70–79	4.24	6.28	1.51	0.79–2.89
>80	1.85	4.59	2.56	1.10–5.97

ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; OR = odds ratio.

DISCUSSION

Older patients have decreased physiologic reserve and a higher number of comorbid conditions and are on more medications compared to younger adults; thus, older persons may have a different prognosis when a new EMS protocol is advocated for OHCA. It is therefore important to evaluate whether new protocols are effective in the geriatric population.

Cardiocerebral resuscitation has been shown to improve neurologically intact survival from cardiac arrest. Kellum et al.[18] demonstrated that neurologically intact survival for OHCA for patients with a shockable rhythm improved from 15% to 39% before and after institution of CCR in two rural Wisconsin EMS systems. This improvement was consistent for a 3-year period before and after the EMS protocol was changed.[18] In 2008, Bobrow et al.[17] reported a before-and-after intention-to-treat analysis in two Arizona EMS systems and found that CCR, also referred to as minimally interrupted cardiac resuscitation, improved survival from 1.8% before to 5.4% (OR = 3.0). Patients in witnessed Vfib/Vtach arrest had improved survival from 4.7% to 17.6% after CCR (OR = 8.6) was instituted.[17] Bobrow et al.[17] also analyzed the statewide SHARE database to compare survival when the protocol met compliance criteria to standard EMS care. He found improvement in overall survival when CCR was compared to other treatment (9.1% vs. 3.8%, OR = 2.7)

Table 4
Survival After Standard ACLS Versus CCR for Vfib/Vtach Arrests Only, Stratified by Age Groups

| Age (yr) | Percent Survival | | OR | 95% CI |
	Standard ACLS	CCR		
<40	16.67	63.64	8.75	1.80–42.80
40–49	20.00	48.48	3.76	1.40–10.08
50–59	12.15	23.88	2.27	1.02–5.02
60–69	18.13	31.91	2.09	1.00–4.38
70–79	14.60	25.00	1.95	0.84–4.54
>80	6.52	19.05	3.37	0.92–12.50

ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; OR = odds ratio; Vfib = ventricular fibrillation; Vtach = ventricular tachycardia.
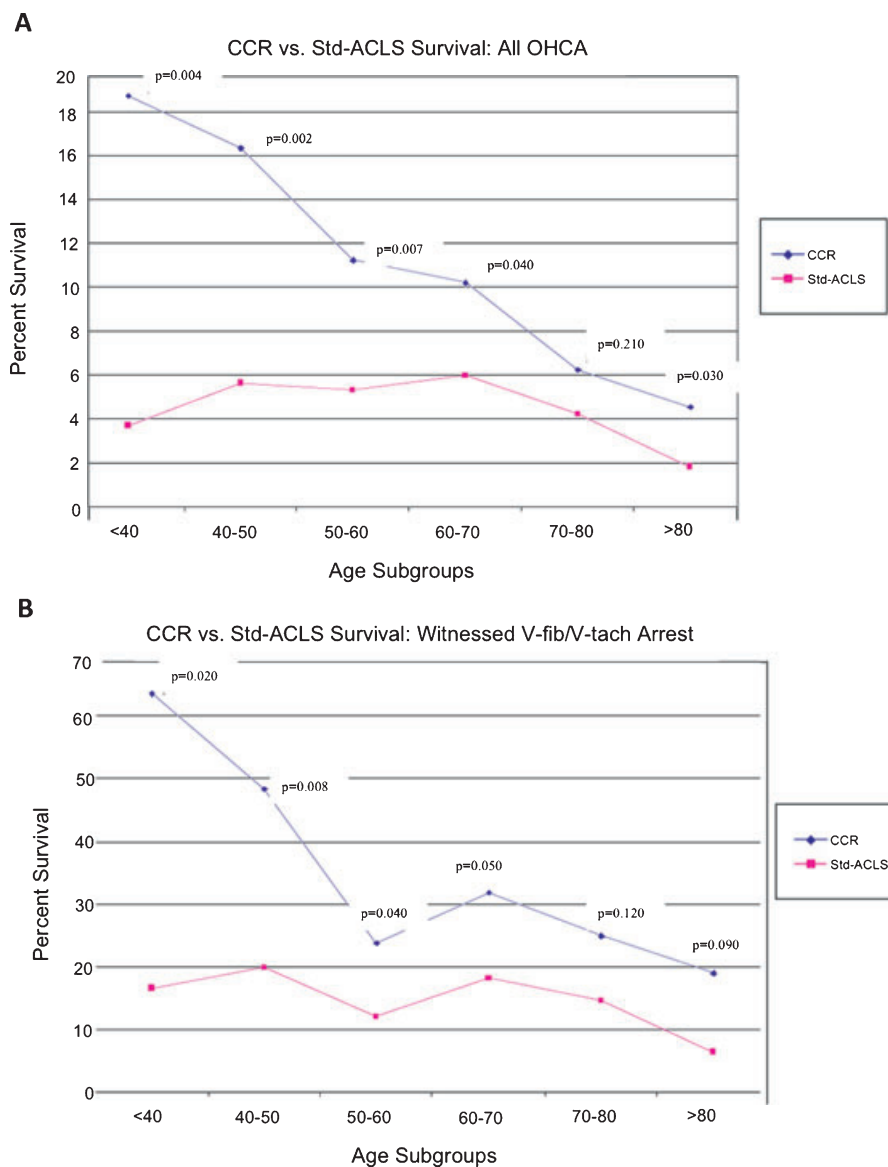
A

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Figure 2. (A) All out-of-hospital cardiac arrests. (B) Subgroup of witnessed Vfib/Vtach arrest. ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; OHCA = out of hospital cardiac arrest; V-fib = ventricular fibrillation; V-tach = ventricular tachycardia.

and survival of patients in witnessed VF arrest (28.4% vs. 11.9%, OR = 3.4).

Our data show that CCR, with minimally interrupted chest compressions, is associated with an overall survival benefit, and a benefit across all age groups. Those patients less than 40 years had the largest mortality

benefit. A possible explanation is that this subgroup of patients had fewer comorbid conditions, better cardiac conditioning, and greater physiologic reserve. The survival benefit of CCR trended downward with age, with a nadir in the 70- to 79-years age group. However, some benefit was regained in the ≥80 years age group.

Table 5
ORs of Independent Predictors in SHARE Registry, by Age Category

	<40 OR	40–49 OR (p-value)	50–59 OR (p-value)	60–69 OR (p-value)	70–79 OR (p-value)	≥80 OR (p-value)
Witnessed arrest	2.1 (0.50)	1.8 (0.51)	1.4 (0.58)	6.9 (0.02)	5.7 (0.04)	4.1 (0.09)
VF/VT	7.1 (0.08)	37 (0.002)	6.5 (0.009)	7.1 (0.002)	6.6 (0.008)	5.6 (0.02)
Response time (min)	0.39 (0.07)	0.82 (0.33)	0.95 (0.66)	0.93 (0.60)	0.86 (0.36)	0.88 (0.53)
Agonal respiration	8.7 (0.16)	6.8 (0.05)	4.8 (0.005)	5.5 (0.005)	6.7 (0.004)	1.4 (0.77)

OR = odds ratio; SHARE = Save Hearts in Arizona Registry and Education; VF/VT = initial rhythm ventricular fibrillation or tachycardia.

Table 6
Neurologic Outcome

	CCR		ACLS		
Age (yr)	Good (CPC 1, 2)	Bad (CPC 3,4)	Good (CPC 1, 2)	Bad (CPC 3, 4)	Totals Number of Patients
<40	5	1	4	0	10
40–49	10	0	6	2	18
50–59	13	0	14	6	33
60–69	13	0	26	2	41
70–79	11	0	17	1	29
>80	5	1	8	2	16

ACLS = advanced cardiac life support; CCR = cardiocerebral resuscitation; CPC = cerebral performance category.

Previous cardiovascular studies have described a similar J-shaped curve, owing to a resilience "survival effect" in elder patients ≥80 years.[30,31] For patients who received CCR, there were several strong predictors of survival. Witnessed arrest with Vfib/Vtach, presence of agonal respirations, and early response time were statistically significant predictors of survival and held across each group.

Although insufficient power existed to detect improved neurologic function between the age groups, there was an overall improvement in neurologic outcome with CCR. This is likely a reflection of the improved survival seen with CCR. As reported previously, the vast majority of patients who survive to hospital discharge are neurologically intact; 96% of all survivors in both groups had good CPC scores.[17] We speculate that most patients who have severe neurologic deficits die in the hospital. It is also possible that there is less cerebral ischemia with CCR, as there are fewer overall interruptions, and less positive pressure ventilation.

LIMITATIONS

This study was a retrospective analysis of a cardiac arrest database, limiting our ability to invoke causality. A randomized controlled trial would be optimal to determine the effect of CCR on survival across various age groups. As a result, a number of factors, such as adjuncts for CPR that may have influenced the results, could not be controlled. The study assessed patients who received CCR by defined criteria. The criteria were assessed based on EMS reports, and independent confirmation of compliance criteria was not obtained. Because there is no way to blind EMS providers to the treatment used, there also may have been a Hawthorne effect, in which the medics tried harder to resuscitate patients because they were using a new protocol or selected patients for CCR who had a better prognosis for survival. We note that in the study by Kellum et al., improvement in neurologically intact survival persisted for 3 years, lessening the concern about the selection bias.[18]

Postresuscitation care of patients who survive OHCA, including therapeutic hypothermia and early percutaneous coronary intervention, are important determinants of survival and neurologic outcomes.[8,9]

We could not control for postresuscitation care in this analysis, although we know at the time of this report very few hospitals in the database had protocols for therapeutic hypothermia post–cardiac arrest. Finally, only 72% of the 204 survivors could be reached for neurologic assessment. Neurologic assessment was also limited by the use of the CPC scale. Although this scale has been used in studies of cardiac arrest, future research should investigate neurologic outcomes by age using more comprehensive neurologic testing and compare baseline and postarrest neuropsychological function.

CONCLUSIONS

Cardiocerebral resuscitation is associated with better rates of survival and overall neurologic outcome than standard advanced cardiac life support treatment for out-of-hospital cardiac arrest, even across age groups. When controlled for age, several variables including witnessed arrest, ventricular fibrillation or tachycardia, presence of agonal respirations, and early response time were statistically significant predictors of survival. Older patients benefit from cardiocerebral resuscitation, and those greater than 80 years old show a marked survival benefit with neurologic preservation. Further research should be done to investigate the overall public health benefit of cardiocerebral resuscitation.

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